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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,557	06/04/2007	Maher Kalaji	31229-232367	4750
26694	7590	05/26/2010	EXAMINER	
VENABLE LLP P.O. BOX 34385 WASHINGTON, DC 20043-9998				DINH, BACH T
ART UNIT		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/582,557	KALAJI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	BACH T. DINH	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 17 March 2010.  
 2a) This action is **FINAL**.                            2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-27 is/are pending in the application.  
 4a) Of the above claim(s) 17-27 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-16 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 09 June 2006 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>06/09/2006</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application
	6) <input type="checkbox"/> Other: _____ .

**DETAILED ACTION**

***Summary***

1. This is the response to the communication filed on 03/25/2010.
2. Claims 1-27 are currently pending with claims 17-27 are withdrawn from consideration in view of Applicant's response to the election/restriction.
3. Claims 1-16 have been fully considered.

***Election/Restrictions***

4. Applicant's election without traverse of group I, claims 1-16 in the reply filed on 03/25/2010 is acknowledged.
5. Applicant's election of group I, claims 1-16 in the reply filed on 03/25/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

***Information Disclosure Statement***

6. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored

in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a). In instant case, references CA-CG listed in the IDS filed on 06/09/2006 have not been considered for copies of such references were not provided by the Applicant.

7. The information disclosure statement filed 06/09/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Specifically, references CA-CG that are lined through by the examiner have not been considered for Applicant fails to provide copies for such references.

***Request for Information***

8. Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to

the examination of this application. This information request includes the following information as described in the paragraph 9 below.

9. In response to this requirement, please provide copies of each publication which any of the applicants authored or co-authored and which describe the disclosed subject matter of the nitroreductase enzyme that is modified to include the terminal cysteine residues; most notably, the reference “Poster 50: The Development of an Amperometric Enzyme Sensor for the Detection of Explosives” Posters of the 2003 Younger European Chemists’ Conference” available on 08/26/2003 as cited in the international search report submitted on 06/09/2006. In order for such reference to be cited in the international search report, such reference must be made public. Therefore, Applicant is respectfully requested to submit a copy for the above reference and references CA-CG as listed in the IDS filed on 06/09/2006.

10. The fee and certification requirements of 37 CFR 1.97 are waived for those documents submitted in reply to this requirement. This waiver extends only to those documents within the scope of this requirement under 37 CFR 1.105 that are included in the applicant’s first complete communication responding to this requirement. Any supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 CFR 1.105 are subject to the fee and certification requirements of 37 CFR 1.97.

11. The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained may be accepted as a complete reply to the requirement for that item.

12. This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Willner et al. (US 5,443,701) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claims 1-4 and 6-7, Willner discloses a sensing device (figure 1) comprising an electrode 1 comprising a noble metal layer (9:29-37, gold electrode), on which a layer 4 of glutathione reductase (9:46-50) is immobilized on the gold electrode (Abstract). Shah discloses that glutathione reductase catalyzes nitroaromatic compounds (3:18-35); therefore, the glutathione reductase is a nitroreductase enzyme.

Addressing claim 5, Willner discloses the biological material comprises a plurality of sulphur-containing functional groups (figures 20 and 22).

Addressing claim 9, Willner discloses the electrode comprises a semi-permeable membrane that encloses the electrode and is permeable to the analyte (5:62-65);

therefore, the immobilized enzyme is also covered by the semi-permeable membrane or the fluid permeable cover layer.

***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Grove et al. (WO 03/018788) and Shah et al. (US 5,777,190).

Addressing claim 8, it is noticed from the originally filed specification the SEQ ID1 and SEQ ID2 refer to the nfnB gene in *E. coli* and pnrA gene in *P. putida*, respectively.

Furthermore, the limitation of current claim is drawn to the process of making the nitroreductase enzyme, which does not further structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the claim is treated

as nitroreductase enzyme encoded by either the *nfnB* gene or *pnrA* gene according to the originally filed specification.

Willner is silent regarding the nitroreductase enzyme is encoded by either the *nfnB* gene or *pnrA* gene.

Grove discloses nitroreductase enzyme; wherein, the nitroreductase enzyme is encoded by the *nfsB* gene or *nfnB* gene (page 2 line 16 to page 3 line 19).

Shah discloses using nitroreductase enzyme to control the reduction of nitroaromatic compounds (1:13-15).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the enzyme of Willner with the nitroreductase enzyme as disclosed by Grove because the nitroreductase enzyme of Grove, which reduces nitroaromatic compounds, would allow one to measure explosives such as TNT (Shah, 2:31-44).

18. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Matsumoto et al. (US 5,795,774) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claim 10, Willner is silent regarding the cover layer comprises a polycarbonate or polyacrylate material.

Matsumoto discloses a biosensor; wherein, polycarbonate is used as a layer for allowing the diffusion of analyte while restricting the diffusion of macromolecules (2:15-31).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the membrane of Willner with the polycarbonate material of

Matsumoto because the polycarbonate material restricts the diffusion of macromolecules while allowing the diffusion of the analyte; thereby, increasing the range of concentrations which the sensor could be used to measure (Matsumoto, 2:22-26).

19. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Saini et al. (US 5,521,101) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claims 11-12, Willner is silent regarding the noble metal layer is mounted on an insulating substrate and is connected to a surface not comprising the biological material, to one or more layers of conductive, semi-conductive or insulating material. Saini discloses a sensor for measuring TNT like that of Willner; wherein, the gold electrodes (9:65-67) are mounted on an insulating substrate 4 (10:9, quartz substrate) or a surface not comprising the biological material.

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the device of Willner with the insulating substrate in the manner disclosed by Saini because the insulating substrate would provide support for the gold electrode (Saini, figure 1, 10:8-9).

20. Claims 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claim 13, the limitation of current claim is drawn to the process of forming the biological material on the noble metal layer, which does not further structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the limitation of current is treated as a layer of nitroreductase is attached to the gold layer via a plurality of cysteine residues at a location on the enzyme that does not interfere with the activity of the enzyme.

Willner discloses using thiol groups for binding the nitroreductase enzyme to the gold electrode (figures 20 and 22).

Willner is silent regarding a plurality of cysteine residues on the enzyme at a location that does not interfere with the enzyme activity is used for binding the enzyme to the gold layer.

Ruger discloses an electrochemical sensor; wherein, the enzyme is modified at the N-terminal attachment with a plurality of cysteine residues (4:13-24) at a location that does not interfere with the enzymatic activity (4:45-49) for binding the enzyme to the supporting material of gold or platinum (3:1-9).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the sensing device of Willner by modifying the nitroreductase enzyme with the plurality of cysteine residues at a location that does not interfere with the enzyme activity in the manner disclosed by Ruger because the plurality of cysteine residues would enhance the bond between the nitroreductase enzyme and the electrode, providing the thiol binding groups required by Willner and provide high covering density of enzyme coupled with high conductivity and sensitivity (Ruger, 2:24-29).

Addressing claim 16, Willner discloses the nitroreductase is operably associated with an electron mediator (5:47-57).

21. Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) as applied to claims 13 and 16 above, and further in view of Grove et al. (WO 03/018788) and Shah et al. (US 5,777,190).

Addressing claims 14-15, it is noticed from the originally filed specification that the SEQ ID3 is the nfnB gene with genetic sequence to express a 6 cysteine residues inserted at the N-terminal end (page 7 lines 23-29 of the specification) and the SEQ ID5 is the pnrA gene with genetic sequence to express a 6 cysteine residues inserted at the N-terminal end (page 7 line 31 to page 8 line 4). Furthermore, SEQ ID4 and SEQ ID6 are the nitroreductase enzymes as the translation products of SEQ ID3 and SEQ ID5, respectively (page 8 lines 6-9). In other words, SEQ ID4 is the nitroreductase enzyme expressed by the nfnB gene with a six cysteine residues attached at the N-terminal; likewise, SEQ ID6 is the nitroreductase enzyme expressed by the pnrA gene with a six cysteine residues attached at the N-terminal. Additionally, the limitation of current claim is drawn to the process of binding the nitroreductase enzyme to the gold electrode, which does not structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the limitation of claims 14 and 15 in light of claim 13 is treated as the nitroreductase enzyme expressed by the nfnB gene or pnrA gene is attached

to the gold electrode via the six cysteine residues provided at the N-terminal of the nitroreductase enzyme.

Willner is silent regarding the nitroreductase enzyme is encoded by either the nfnB gene or pnrA gene having six cysteine residues attached at the N-terminal for binding the enzyme to the gold electrode.

Grove discloses nitroreductase enzyme; wherein, the nitroreductase enzyme is encoded by the nfsB gene or nfnB gene (page 2 line 16 to page 3 line 19).

Shah discloses using nitroreductase enzyme to control the reduction of nitroaromatic compounds (1:13-15).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the enzyme of Willner with the nitroreductase enzyme as disclosed by Grove because the nitroreductase enzyme of Grove, which reduces nitroaromatic compounds, would allow one to measure explosives such as TNT (Shah, 2:31-44).

Ruger discloses an electrochemical sensor; wherein, the enzyme is modified at the N-terminal attachment with a plurality of cysteine residues (4:13-24) at a location that does not interfere with the enzymatic activity (4:45-49) for binding the enzyme to the supporting material of gold or platinum (3:1-9).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the sensing device of Willner by modifying the nitroreductase enzyme disclosed by Grove with the plurality of cysteine residues at the N-terminal in the manner disclosed by Ruger because the plurality of cysteine residues would enhance the bond between the nitroreductase enzyme and the electrode, providing the thiol binding groups

required by Willner and provide high covering density of enzyme coupled with high conductivity and sensitivity (Ruger, 2:24-29). Additionally, it would have been obvious for one with ordinary skill in the art to modify the N-terminal of the nitroreductase enzyme of Grove with six cysteine residues because Ruger already discloses the inclusion of a plurality of cysteine residues at the N-terminal; therefore, absent of contrary support to show criticality, choosing to incorporate six cysteine residues is obvious as a matter of engineering choice and is well within the technical grasp of one with ordinary skill in the art. Furthermore, the amount of cysteine residues at the N-terminal affects the bond between the enzyme and the electrode; therefore, one would have arrived at the six cysteine residues at the N-terminal of the nitroreductase enzyme when performing routine experiment with the amount of cysteine residues incorporated at the N-terminal of the enzyme in order to optimize the bond between the enzyme and the electrode.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BACH T. DINH whose telephone number is (571)270-5118. The examiner can normally be reached on Monday-Friday EST 7:00 A.M-3:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam X. Nguyen can be reached on (571)272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nam X Nguyen/  
Supervisory Patent Examiner, Art Unit 1753

BD  
05/20/2010